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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/608,626	06/27/2003	Stephen M. Kelsey	P1467R2P2	4813

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EXAMINER	
SANG, HONG	

ART UNIT	PAPER NUMBER
1643	

DATE MAILED: 09/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/608,626	KELSEY ET AL.	
	Examiner	Art Unit	
	Hong Sang	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 August 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) *7-12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 13-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/29/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

RE: Kelsey et al.

1. Applicant's response filed on 8/29//2006 is acknowledged. New claims 13-19 are added. Claims 7-12 have been withdrawn from further consideration. Claims 1, and 3-5 are amended.

2. Claims 1-6 and 13-19 are under examination.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. The information disclosure statement (IDS) filed on 8/29/06 has been considered. A signed copy is attached hereto.

5. Due to applicants' species election of medulloblastoma and cancellation of species of carcinoma, the claims are examined to the extent that the cancer is medulloblastoma or blastoma.

6. Applicants statement that applicants do not dispute that the word "medulloblastoma" is not expressly recited in 60/141,316 or 10/268,501, and preserve the right to traverse is acknowledged.

Objections Withdrawn

7. The objections to the specification because there is no brief description for Figure 8B and Figure 8C under the "Brief Description of the Drawings" (see page 7, line 10) is withdrawn in view of applicants' arguments.

Rejections Withdrawn

8. The rejection of claims 3-5 under 35 U.S.C. 112, second paragraph, as being indefinite for reciting the terms 2C4 and 4D5 as the sole means of identifying the claimed molecules is withdrawn in view of applicants' amendment to the claims.

9. The rejection of claims 3-5 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement because the specification does not provide evidence that the claimed biological materials are (1) known and readily available to the public; (2) reproducible from the written description is withdrawn in view of applicants' deposit of the claimed antibodies.

10. The rejection of claims 1-6 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement is withdrawn in view of the Grossi's reference submitted in the response.

11. All art rejections and double patenting rejections are withdrawn in view of applicants' amendment to the claims and new grounds of rejections.

New Grounds of Rejections

Claim Rejections - 35 USC § 112, 2nd paragraph

12. Claim 16 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 16 contains the trademark/trade name HERCEPTIN®. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe an antibody and, accordingly, the identification/description is indefinite.

Claim Rejections - 35 USC § 102

13. Claims 13 and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 98/17797 (International Publication Date: 4/30/1998, IDS) as evidenced by Shepard et al. (J. Clinical Immunology, 1991, 11(3), 117-126, IDS).

Claims 13 and 15 are drawn to a method of treating blastoma that express ErbB2 comprising administering a therapeutically effective amount of an antibody which binds

ErbB2 to a patient. The method is further limited wherein the antibody is monoclonal antibody 4D5 or humanized 4D5, and the antibody blocks binding of monoclonal antibody 2C4 to ErbB2.

WO 98/17797 teaches a method of treating a tumor that overexpresses ErbB2 receptor comprising administering to a subject an effective amount of a monoclonal antibody or a humanized antibody such as 7C2, 7F3 and 4D5, wherein the tumor is glioblastoma (see claims 28-31, page 4, lines 22-26, page 5, lines 5-8, page 9 and page 36, lines 9-15). . WO 98/17797 teaches that the antibodies 7C2, 7F3 and 4D5 bind to the extracellular domain of the receptor (see page 9, lines 22-30) and inhibit the ligand from binding the receptor (see column 5, lines 42-43).

The antibodies 7C2, 7F3 and 4D5 block ligand activation of an ErbB receptor and the antibody 7F3 blocks binding of monoclonal antibody 2C4 to ErbB2, as evidenced by Shepard et al.

Shepard et al. teach that the monoclonal antibodies 4D5, 2C4 and 7F3, etc. selectively bind the extracellular domain of ErbB2 (p185/HER2) and inhibit proliferation of human breast and ovarian tumor cells that express ErbB2 (see for example, Table III, page 123). Shepard et al. teach that the antibodies bind tightly to ErbB2, excludes ligand binding, downregulates receptor signaling pathways (see page 124, first paragraph). Shepard et al. teach that the antibody 7F3 blocks binding of monoclonal antibody 2C4 to ErbB2 (see notes of Table III, line 4).

Because glioblastoma is one type of blastoma, therefore, WO 08/17797 teaches every limitation of the claims.

Claim Rejections - 35 USC § 103

14. Claims 1-6 and 13-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 98/17797 (International Publication Date: 4/30/1998, IDS) in view of Schaefer et al. (Oncogene, 1997, 15: 1385-1394, IDS), Carter et al. (Proc. Natl. Acad. Sci. USA, 1992, 89: 4285-4289, IDS), WO 01/00245 A2 (Publication Date: 1/4/2001, IDS), Gilbertson et al. (Clinical Cancer Res. (1999, Nov. 5 (Suppl.), 3737s, Abstract #38, IDS), and as evidenced by Shepard et al. (J. Clinical Immunology, 1991, 11(3), 117-126, IDS).

The interpretations of claims 13 and 15 are set forth above (see paragraph 13).

Claims 1-6, 14, and 16-19 are interpreted as a method of treating medulloblastoma that expresses ErbB2 comprising administering a therapeutically effective amount of an antibody which binds ErbB2 to a patient. The method is further limited wherein the antibody blocks ligand activation of an ErbB receptor, the antibody blocks binding of monoclonal antibody 2C4 to ErbB2, the antibody is monoclonal antibody 4D5 or humanized 4D5, the antibody is a monoclonal 2C4 or humanized 2C4, the antibody is a humanized 4D5 antibody comprising huMab4D5-8 (HERCEPTIN®), and the antibody is a humanized version of monoclonal antibody of 2C4.

The teachings of WO 98/17797 and Shepard are set forth above as they apply to claims 13 and 15.

WO 98/17797 does not teach that the antibody is a humanized 4D5 antibody comprising huMab4D5-8 (HERCEPTIN®), a humanized antibody 2C4, or a humanized

version of monoclonal antibody of 2C4. WO 98/17797 does not teach the tumor is medulloblastoma. However, these deficiencies are made up for in the teachings of Schaefer, Carter and Gilbertson.

Schaefer et al. teach that anti-ErbB2 monoclonal antibodies 2C4 and 4D5 inhibit proliferation of human breast cancer cells MDA-MB-175 and SK-BR-3 by blocking the association of ErbB2 with ErbB3 via blocking gamma-HRG activation of ErbB3 and ErbB3 (Fig. 7). Schaefer et al. teach that these antibodies interfere with the ligand dependent formation of ErbB2-ErbB3 heterodimer complexes (see abstract, lines 20-24, and page 1390, 2nd paragraph)). Schaefer et al. teach that anti-ErbB23 monoclonal antibody 2C4 effectively blocks neuregulin binding and down stream signaling (see page 1390, left column, 2nd paragraph, lines 10-13). Moreover, Schaefer et al. teach that the antibody 2C4, which binds to a different ErbB2 epitope significantly inhibited (76%) cell growth in MDA-MB-175 cells, however, 4D5 shows only a moderate growth inhibition (see page 1390, left column, last section).

Carter et al. teach that the humanized antibody humAb4D5-8 binds $p185^{HER2}$ antigen 250-fold and 3-fold more tightly than humAb4D5-1 and mumAb4D5, respectively. In addition, humAb4D5-8 has potency comparable to the murine antibody in blocking SK-BR-3 cell proliferation. Furthermore, humAb4D5-8 is much more efficient in supporting antibody-dependent cellular cytotoxicity against SK-BR-3 cells than mumAb4D5 (see abstract).

WO 01/00245 A2 teaches humanized antibody 2C4 or humanized version of a monoclonal antibody 2C4 (see the paragraph bridging pages 13 and 14, and Example 3).

Gilbertson et al. teach that ErbB2 receptor represents a potential target for novel therapies in childhood medulloblastoma (see title). Gilbertson et al. teach that the anti-ErbB2 monoclonal antibody Herceptin™ (supplied by Genetech Inc.) significantly inhibited the *in vitro* growth of the two out of the three medulloblastoma cell lines tested (see abstract).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to use the method of WO 98/17797 and the antibodies of Schaefer, Carter or WO 01/00245 (i.e. humAb4D5-8 antibody, monoclonal or humanized 2C4 antibody) to treat medulloblastoma in view of the teachings of Schaefer, Carter, WO 01/00245 and Gilbertson. One would have been motivated to use the method of WO 98/17797 and the antibodies of Schaefer, Carter or WO 01/00245 (i.e. humAb4D5-8 antibody, monoclonal or humanized 2C4 antibody) to treat a medulloblastoma that expresses ErbB2 in a patient because Gilbertson et al. teach the anti-ErbB2 monoclonal antibody Herceptin™ (supplied by Genetech, Inc.) significantly inhibited the *in vitro* growth of medulloblastoma cells and ErbB2 receptor represents a potential target for novel therapies in childhood medulloblastoma, and Schaefer, Carter and WO 01/0245 teach that humAb4D5-8 mAb4D5, monoclonal 2C4 antibody or humanized 2C4 antibody are potent growth inhibitors for tumor cells that express ErbB2 antibody. One of ordinary skill in the art would have a reasonable expectation of

success to use the method of WO 98/17797 and the antibodies of Schaefer, Carter or WO 01/00245 (i.e. humAb4D5-8 antibody, monoclonal 2C4 antibody or humanized 2C4 antibody) to treat a medulloblastoma that expresses ErbB2 in a patient because WO 98/17797 teach that anti-ErbB2 antibodies such as 4D5, and 7F3 can treat glioblastoma (brain cancer), Gilbertson has shown that 4D5 antibody inhibited the growth of medulloblastoma cells *in vitro*, and Schaefer, Carter or WO 01/00245 teach that humAb4D5-8 antibody, monoclonal 2C4 antibody and humanized 2C4 antibody can treat cancer that expresses ErbB2.

Double Patenting

15. Claims 13 and 15 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 7 and 22 of US Patent No. 6,627,196B1. Although the conflicting claims are not identical, they are not patentably distinct from each other.

Claims 13 and 15 and their interpretation are set forth above (see paragraphs 13).

Claims 1, 17 and 22 of US Patent No. 6,627,196B1 are drawn to a method for treatment of a human patient diagnosed with cancer characterized by overexpression of ErbB2 receptor, comprising administering an effective amount of an anti-ErbB2 antibody to the human patient, comprising administering to the patient an initial dose of at least approximately 5mg/kg of the anti-ErbB2 antibody, and administering to the patient in an amount that is approximately the same or less than the initial dose, wherein the

subsequent doses are separated in time from each other by at least two weeks, wherein the cancer is glioblastoma, the antibody is a humanized 4D5 anti-ErbB2 antibody. Because glioblastoma is one type of blastoma, claims 1, 17 and 22 of the US Patent No. 6,627,196B1 anticipate the instant claims 13 and 15.

Claims 13 and 15 directed to an invention not patentably distinct from claims 1, 17 and 22 of commonly assigned US patent No. 6,627,196B1 for the reasons set forth above.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP § 2302). Commonly assigned US Patent No. 6,627,196B1, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications filed on or after November 29, 1999.

Conclusion

16. No claims are allowed.

Applicant's amendment and Applicant's submission of an information disclosure statement under 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.17(p) on 4/19/06 prompted the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a) and 609.04(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hong Sang whose telephone number is (571) 272 8145. The examiner can normally be reached on 8:30am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Hong Sang, Ph.D.
Art Unit 1643
Sept. 15, 2006

LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER